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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/719,990	11/21/2003	Alan Howe	421/73/2	1736

25297 7590 09/14/2009

JENKINS, WILSON, TAYLOR & HUNT, P. A.
Suite 1200 UNIVERSITY TOWER
3100 TOWER BLVD.,
DURHAM, NC 27707

EXAMINER	
FETTEROLF, BRANDON J	

ART UNIT	PAPER NUMBER
1642	

MAIL DATE	DELIVERY MODE
09/14/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/719,990	HOWE, ALAN	
	Examiner	Art Unit	
	BRANDON J. FETTEROLF	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 August 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-14,36,38,39 and 41-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-14,36,38,39 and 41-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/07/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/07/2009 has been entered.

Claims 1-4, 6-14, 36, 38-39, 41-48 are currently pending and under consideration.

Information Disclosure Statement

The Information Disclosure Statement filed on 8/07/2009 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. A signed copy of the IDS is attached hereto.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 36, 38-39 and 47 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. THIS IS A NEW MATTER REJECTION.

Claim 36 has been amended to cite the limitation that the kit comprises a membrane. However, the specification and claims, as originally filed, do not appear to have support for the limitation that a kit comprises a PPDR, a membrane and instructions for using the PPDR. Applicant is required to cancel the new matter in the response to this Office Action. Alternatively,

applicant is invited to provide sufficient written support for the "limitation" indicated above. See MPEP 714.02 and 2163.06

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-2, 4, 6-9, 10 36, 38-39 and 41-45 are rejected under 35 U.S.C. 102(e) as being anticipated by Agnew et al. (US 7,102,005 B2 priority to 5/3/2002).

Agnew et al. teach water soluble phosphate binding compounds and a phosphate-binding solution, wherein the phosphate-binding compounds when present in the binding solution, preferentially bind phosphorylated target molecules (column 30, lines 54-60 and column 51, lines 31-34). With regards to the binding solution, the patent teaches that the binding solution has three critical components: 1) a phosphate-binding compound having the formula $(A)_m(L)_n(B)$, wherein A is a chemical moiety, L is a linker, B is a metal-chelating moiety; 2) a salt comprising a metal ion and 3) an acid (column 30, lines 60-66). With regards to the metal chelating moiety, the patent teaches that metal chelating moieties include, but are not limited to, IDA (for example, column 7, line 65). With regards to the metal ion, the patent teaches that metal ions include, but are not limited to, Al^{3+}, Fe^{3+} and Ga^{3+} (column 18, lines 9-15). With regards to the chemical moiety, the patent teaches that chemical moieties include, labels such as biotin (column 22, line 5-7 and column 25, line 6). With regards to the phosphorylated target molecules, the patent teaches that phosphorylated compounds include, but are not limited to, membrane bound phosphoproteins (see column 94, Example 29 for example). Moreover, the patent teaches various method of producing the phosphate binding compound and contacting a binding solution comprising said phosphate binding compound with a membrane bound phosphoprotein (see for example, column 999, Example 35 and Example 29). In

addition, the patent teach a kit comprising a phosphate binding compound, a binding solution, a protein binding support and an appropriate affinity reagent (column 71, liens 30-42).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 46-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Agnew et al. (US 7,102,005 B2 priority to5/3/2002), as applied above to claims 1-2, 4, 6-9, 10 36, 38-39 and 41-45.

Agnew et al. teach water soluble phosphate binding compounds and a phosphate-binding solution, wherein the phosphate-binding compounds when present in the binding solution, preferentially bind phosphorylated target molecules (column 30, lines 54-60 and column 51, lines 31-34). With regards to the binding solution, the patent teaches that the binding solution has three critical components: 1) a phosphate-binding compound having the formula (A)m(L)n(B), wherein A is a chemical moiety, L is a linker, B is a metal-chelating moiety; 2) a salt comprising a metal ion and 3) an acid (column 30, lines 60-66). With regards to the metal chelating moiety, the patent teaches that metal chelating moieties include, but are not limited to, IDA (for example, column 7, line 65). With regards to the metal ion, the patent teaches that metal ions include, but are not limited to,

Al3+, Fe3+ and Ga3+ (column 18, lines 9-15). With regards to the chemical moiety, the patent teaches that chemical moieties include, labels such as biotin (column 22, line 5-7 and column 25, line 6). With regards to the phosphorylated target molecules, the patent teaches that phosphorylated compounds include, but are not limited to, membrane bound phosphoproteins (see column 94, Example 29 for example). With regards to the binding solution, the patent teaches that the pH of the binding solution is between 3 to about 6. Moreover, the patent teaches various method of producing the phosphate binding compound and contacting a binding solution comprising said phosphate binding compound with a membrane bound phosphoprotein (see for example, column 999, Example 35 and Example 29). In addition, the patent teach a kit comprising a phosphate binding compound, a binding solution, a protein binding support and an appropriate affinity reagent (column 71, liens 30-42).

Agnew et al .do not explicitly teach that the pH of the binding solution is between 5 to about 7.

However, the pH of the binding solution taught by Agnew et al. of about 3 to about 6 clearly overlaps the claimed binding solution of between 5 to about 7. Accordingly, the courts have found that in the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a prima facie case of obviousness exists. In re Wertheim, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); In re Woodruff, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990).

Claims 3 and 41-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Agnew et al. (US 7,102,005 B2 priority to5/3/2002), as applied above to claims 1-2, 4, 6-9, 10 36, 38-39 and 41-45 in further view of Posewitz (Anal. Chem. 1999, 71: 2883-2892).

Agnew et al. teach water soluble phosphate binding compounds and a phosphate-binding solution, wherein the phosphate-binding compounds when present in the binding solution, preferentially bind phosphorylated target molecules (column 30, lines 54-60 and column 51, lines 31-34). With regards to the binding solution, the patent teaches that the binding solution has three critical components: 1) a phosphate-binding compound having the formula (A)m(L)n(B), wherein A is a chemical moiety, L is a linker, B is a metal-chelating moiety; 2) a salt comprising a metal ion and 3) an acid (column 30, lines 60-66). With regards to the metal chelating moiety, the patent teaches that metal chelating moieties include, but are not limited to, IDA (for example, column 7, line 65).

With regards to the metal ion, the patent teaches that metal ions include, but are not limited to, Al3+, Fe3+ and Ga3+ (column 18, lines 9-15). With regards to the chemical moiety, the patent teaches that chemical moieties include, labels such as biotin (column 22, line 5-7 and column 25, line 6). With regards to the phosphorylated target molecules, the patent teaches that phosphorylated compounds include, but are not limited to, membrane bound phosphoproteins (see column 94, Example 29 for example). With regards to the binding solution, the patent teaches that the pH of the binding solution is between 3 to about 6. Moreover, the patent teaches various method of producing the phosphate binding compound and contacting a binding solution comprising said phosphate binding compound with a membrane bound phosphoprotein (see for example, column 999, Example 35 and Example 29). In addition, the patent teach a kit comprising a phosphate binding compound, a binding solution, a protein binding support and an appropriate affinity reagent (column 71, liens 30-42).

Agnew et al .do not explicitly teach that metal chelating moiety is NTA.

Posewitz et al. teach the quadridentate metal binding ligand nitriloacetic acid (NTA) is selective for retaining phosphorylated proteins.

Thus, it would have been prima facie obvious to one of skill in the art at the time the invention was made to combine the teachings of the reference so as to substitute the metal chelating ligand as taught by Agnew for NTA in view of the teachings of Posewitz et al. One would have been motivated to do so because as taught by Posewitz, NTA is selective for retaining phosphorylated proteins. Thus, one would have a reasonable expectation of success that by substituting the metal chelating ligand as taught by Agnew for NTA in view of the teachings of Posewitz et al., one would achieve more selective identification of phosphorylated proteins.

Claims 1-2, 4, 6-14, 36, 38-39 and 41-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Etheshami (1996 "Synthesis and Characterization of Bioaffinity Interactive Heterobifunctional Polyethylene Glycols", Ph.D. dissertation, University of Arizona, of record), as evidenced by Ehteshami *et al.* (J. Molecular Recognition 1996; 9: 733-737, *of record*), in view of Agnew et al. (US 7,102,005 B2 priority to5/3/2002).

Etheshami et al. disclose (page 83 and 89) a conjugate comprising a polydentate chelator moiety and a detectable moiety conjugated to the polydentate chelator moiety via a PEG spacer

group. With regards to the polydentate chelator moiety, the reference teaches (page 89) that the chelator is iminodiacetic acid (IDA). With regards to the detectable moiety, Etheshami et al. teach (page 83) that the detectable moiety is biotin. The reference also teaches (page 83-84) a method of synthesizing the conjugate comprising contacting iminodiacetic acid (IDA) with a molar excess of NHS-biotin under conditions wherein the biotin is transferred to IDA to form the chelator-detectable moiety complex. Etheshami further teaches (page 89) that the synthesis step further comprises mixing the IDA-PEG-Biotin conjugate in a metal ion containing solution, wherein the conjugate and metal ion are present in an equimolar concentration, i.e. 1:1. Etheshami discloses (page 123, Chapter 5) a heterobifunctional poly (ethylene) glycol derivative having the structure biotin-PEG-IDA and its application in protein purification and characterization using a two phase system. Moreover, the dissertation teaches the effect of IDA in these biochelates in a two phase system for the separation of hemoglobin, a protein with a large number of surface accessible histidines that can interact with the immobilized metal ions and no affinity for biotin (page 126). In particular, the reference teaches (page 89) that the chelator is iminodiacetic acid (IDA) and the metal is Cu2+. Lastly, the reference further teaches that the conjugates are useful for immobilized metal affinity chromatography (IMAC) (abstract, page 20). Thus, while Etheshami does not specifically teach that the conjugate is soluble in an aqueous solution, the claimed functional limitation would be an inherent property of reference conjugate because as evidenced by Ehteshami *et al.* (supra), the presence of the PEG spacer between the chelator-metal ion moiety and the detectable label provides water solubility (abstract and page 733, *Introduction*, 1st column, lines 14-15).

As such, Etheshami teach a heterobifunctional conjugate comprising a polydentate chelator, a linker and a detectable moiety. However, Etheshami et al. does not explicitly teach that heterobifunctional conjugate binds to a membrane bound phosphorylated protein, wherein the metal ion is Fe^{3+}, Al^{3+}, Yb^{3+} or Ga^{3+} or that the binding solution is in a pH range of 5 to 7.0. Nor does Etheshami teach a kit.

Agnew et al. teach water soluble phosphate binding compounds and a phosphate-binding solution, wherein the phosphate-binding compounds when present in the binding solution, preferentially bind phosphorylated target molecules (column 30, lines 54-60 and column 51, lines 31-34). With regards to the binding solution, the patent teaches that the binding solution has three critical components: 1) a phosphate-binding compound having the formula (A)m(L)n(B), wherein A

is a chemical moiety, L is a linker, B is a metal-chelating moiety; 2) a salt comprising a metal ion and 3) an acid (column 30, lines 60-66). With regards to the metal chelating moiety, the patent teaches that metal chelating moieties include, but are not limited to, IDA (for example, column 7, line 65). With regards to the metal ion, the patent teaches that metal ions include, but are not limited to, Al3+, Fe3+ and Ga3+ (column 18, lines 9-15). With regards to the chemical moiety, the patent teaches that chemical moieties include, labels such as biotin (column 22, line 5-7 and column 25, line 6). With regards to the phosphorylated target molecules, the patent teaches that phosphorylated compounds include, but are not limited to, membrane bound phosphoproteins (see column 94, Example 29 for example). With regards to the binding solution, the patent teaches that the pH of the binding solution is between 3 to about 6. Moreover, the patent teaches various method of producing the phosphate binding compound and contacting a binding solution comprising said phosphate binding compound with a membrane bound phosphoprotein (see for example, column 999, Example 35 and Example 29). In addition, the patent teach a kit comprising a phosphate binding compound, a binding solution, a protein binding support and an appropriate affinity reagent (column 71, liens 30-42).

Thus, it would have been prima facie obvious to one of skill in the art at the time the invention was made to combine the teachings of the reference so as to use the heterobifunctional conjugate as taught by Etheshami et al. to detect phosphorylated proteins and substitute the metal ion and adjust the pH in view of the teachings of Agnew et al. One would have been motivated to do so because the prior art references represent analogous teachings of detecting proteins using a heterobifunctional conjugate comprising a label, a linker and a metal chelating moiety. Moreover, as taught by Agnew et al., substitution of the metal ion for Al3+, Fe3+ and Ga3 and adjustment of the binding solution pH enables the heterobifunctional reagent to detect phosphorylated proteins on a membrane. Accordingly, one would have a reasonable expectation of success that by using the heterobifunctional conjugate as taught by Etheshami et al. to detect phosphorylated proteins and substitute the metal ion and adjust the pH in view of the teachings of Agnew et al., one would achieve a composition for the detection of phosphorylated proteins.

Moreover, it would have been prima facie obvious to one of skill in the art at the time the invention was made to package the chelated metal conjugate as taught by Etheshami in view of Agnew et al. into a kit useful for the detection of a polypeptide fragments because a kit would insure

standardization of reagents for testing. One of ordinary skill in the art at the time the invention was made would have been motivated to make a kit useful for the detection of polypeptides because standard kits enhance the probability of reproducibility and efficiency of the detection process, and further, provide for increased marketability, convenience, reliability and economy.

Claims 3 and 41-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Etheshami (1996 "Synthesis and Characterization of Bioaffinity Interactive Heterobifunctional Polyethylene Glycols", Ph.D. dissertation, University of Arizona, of record), as evidenced by Ehteshami *et al.* (J. Molecular Recognition 1996; 9: 733-737, *of record*), in view of Agnew et al. (US 7,102,005 B2 priority to5/3/2002) as applied above to claims 1-2, 4, 6-14, 36, 38-39 and 41-48 in further view of Posewitz (Anal. Chem. 1999, 71: 2883-2892).

Etheshami et al. in view of Agnew et al. teach a composition comprising a membrane bound phosphoprotein, the metal chelating moiety IDA, a metal ion selected from the group consisting of Al3+, Fe3+ and Ga3 and a binding solution having a pH between 3 to about 6.

Estheshami et al. in view of Agnew et al. do not explicitly teach that metal chelating moiety is NTA.

Posewitz et al. teach the quadridentate metal binding ligand nitriloacetic acid (NTA) is selective for retaining phosphorylated proteins.

Thus, it would have been prima facie obvious to one of skill in the art at the time the invention was made to combine the teachings of the reference so as to substitute the metal chelating ligand as taught by Etheshami et al. in view of Agnew for NTA in view of the teachings of Posewitz et al. One would have been motivated to do so because as taught by Posewitz, NTA is selective for retaining phosphorylated proteins. Thus, one would have a reasonable expectation of success that by substituting the metal chelating ligand as taught by Etheshami et al. in view of Agnew for NTA in view of the teachings of Posewitz et al., one would achieve more selective identification of phosphorylated proteins

Therefore, No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BRANDON J. FETTEROLF whose telephone number is (571)272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Brandon J Fetterolf
Primary Examiner
Art Unit 1642

/Brandon J Fetterolf/
Primary Examiner, Art Unit 1642